Docket No. JAB-1677

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Paul A.J. Janssen et al.

Serial No. : Art Unit:

Filed : Examiner:

For : SUBSTITUTED DIAMINO-1,3,5-TRIAZINE DERIVATIVES

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on

November 15, 2001

(Date)

Mary A. Appollina

Name of applicant, assignee, or Registered Representative

Mary A. Appollina

(Signature)

November 15, 2001

(Date of Signature)

Assistant Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Dear Sir:

Please amend the above-identified application as follows and consider the following remarks.

In the Specification:

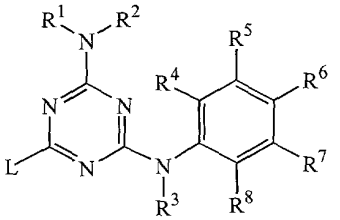
On page 1, between the Title of the Invention and line 4 of the specification, add the following new paragraph:

--This application is a divisional of prior application U.S. Serial No. 09/938,602, filed September 26, 1997, which claims priority from United States provisional application Serial No. 60/027,260, filed October 1, 1996, the contents of which are hereby incorporated by reference.--

In the Claims:

Cancel claims 5, 7-10, 13 and 15 without prejudice, amend claims 1-4, 6, 11-12, 14 and 16-17, and add new claim 18 as follows.

1. A compound of formula



(I')

a pharmaceutically acceptable acid addition salt or a stereochemically isomeric form thereof, wherein

R^1 and R^2 are each independently selected from hydrogen; hydroxy; amino; C_{1-6}alkyl; C_{1-6}alkyloxy; C_{1-6}alkylcarbonyl; C_{1-6}alkyloxycarbonyl; Ar^1; mono- or di(C_{1-6}alkyl)amino; mono- or di(C_{1-6}alkyl)aminocarbonyl; dihydro-2(3*H*)-furanone; C_{1-6}alkyl substituted with one or two substituents each independently selected from amino, imino, aminocarbonyl, aminocarbonylamino, hydroxy, hydroxyC_{1-6}alkyloxy, carboxyl, mono- or di(C_{1-6}alkyl)amino, C_{1-6}alkyloxycarbonyl and thienyl; or

R^1 and R^2 taken together may form pyrrolidinyl, piperidinyl, morpholinyl, azido or mono- or di(C_{1-6}alkyl)aminoC_{1-4}alkylidene;

R^3 is hydrogen, Ar^1, C_{1-6}alkylcarbonyl, C_{1-6}alkyl, C_{1-6}alkyloxycarbonyl, C_{1-6}alkyl substituted with C_{1-6}alkyloxycarbonyl; and

R^4, R^5, R^7 and R^8 are each independently selected from hydrogen, hydroxy, halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano,

aminocarbonyl, nitro, amino, trihalomethyl or trihalomethyloxy ;

R^6 is aminocarbonyl; or

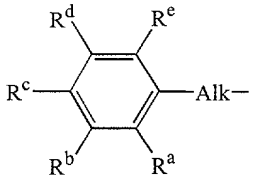
L is C_{1-10}alkyl substituted with one or two substituents independently selected from C_{3-7}cycloalkyl; indolyl or indolyl substituted with one, two, three or four substituents each independently selected from halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, C_{1-6}alkylcarbonyl; phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, hydroxy, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, C_{1-6}alkylcarbonyl; and,

Ar^1 is phenyl, or phenyl substituted with one, two or three substituents each independently selected from halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, nitro or trifluoromethyl.

2. A compound according to claim 1 wherein R^1 and R^2 are each independently selected from hydrogen, C_{1-6}alkyl, Ar^1 or mono- or di(C_{1-6}alkyl)aminocarbonyl; or R^1 and R^2 taken together may form pyrrolidinyl, piperidinyl or morpholinyl;

R^3 is hydrogen, C_{1-6}alkyl or Ar^1; and Ar^1 is phenyl, or phenyl substituted with one, two or three substituents each independently selected from halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, nitro or trifluoromethyl; and

L is a radical of formula



wherein Alk is C_{1-6}alkanediyl;

R^a, R^b, R^c, R^d, R^e, R^4, R^5, R^7 and R^8 are each independently selected from hydrogen, halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl or trihalomethyloxy; or

R^a and R^b taken together may form a bivalent radical of formula

-CH=CH-NR^9- (a-1),

-NR^9-CH=CH- (a-2),

wherein R^9 is hydrogen or C_{1-4}alkyl.

3. A compound according to claim 2 wherein L is C_{3-10}alkenyl or C_{1-2}alkyl substituted with one or two substituents independently selected from C_{3-7}cycloalkyl; indolyl or indolyl substituted with one, two, three or four substituents each independently selected from halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, C_{1-6}alkylcarbonyl; phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, hydroxy, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, C_{1-6}alkylcarbonyl.

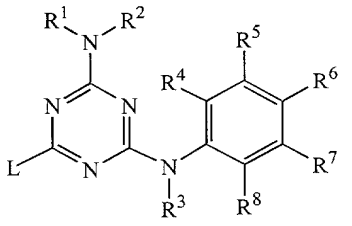
4. A compound according to claim 3 wherein L is 2,6-dichlorophenylmethyl.

6. A compound according to claim 4 wherein NR^1R^2 is other than amino.

11. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically active amount of a compound as claimed claim 1.

12. A process for preparing a pharmaceutical composition comprising intimately mixing a therapeutically effective amount of a compound as claimed in claim 1 with a pharmaceutically acceptable carrier.

14. The combination of a compound of formula (I)



(I)

wherein R^1 and R^2 are each independently selected from hydrogen; hydroxy; amino; C_{1-6}alkyl; C_{1-6}alkyloxy; C_{1-6}alkylcarbonyl; C_{1-6}alkyloxycarbonyl; Ar^1; mono- or di(C_{1-6}alkyl)amino; mono- or di(C_{1-6}alkyl)aminocarbonyl; dihydro-2(3*H*)-furanone; C_{1-6}alkyl substituted with one or two substituents each independently selected from amino, imino, aminocarbonyl, aminocarbonylamino, hydroxy, hydroxyC_{1-6}alkyloxy, carboxyl, mono- or di(C_{1-6}alkyl)amino, C_{1-6}alkyloxycarbonyl and thienyl; or

R^1 and R^2 taken together may form pyrrolidinyl, piperidinyl, morpholinyl, azido or mono- or di(C_{1-6}alkyl)aminoC_{1-4}alkylidene;

R^3 is hydrogen, Ar^1, C_{1-6}alkylcarbonyl, C_{1-6}alkyl, C_{1-6}alkyloxycarbonyl, C_{1-6}alkyl substituted with C_{1-6}alkyloxycarbonyl; and

R^4, R^5, R^7 and R^8 are each independently selected from hydrogen, hydroxy, halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl or trihalomethyloxy;

R^6 is selected from cyano or aminocarbonyl;

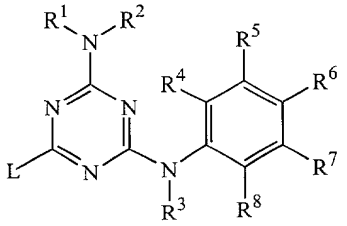
L is C_{1-10}alkyl; C_{3-10}alkenyl; C_{3-10}alkynyl; C_{3-7}cycloalkyl; or

L is C_{1-10}alkyl substituted with one or two substituents independently selected from C_{3-7}cycloalkyl; indolyl or indolyl substituted with one, two, three or four substituents each independently selected from halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, C_{1-6}alkylcarbonyl; phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, hydroxy, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, C_{1-6}alkylcarbonyl; and,

Ar^1 is phenyl, or phenyl substituted with one, two or three substituents each independently selected from halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, nitro or trifluoromethyl;

and another antiretroviral compound.

16. A product containing (a) a compound of formula (I)



(I)

wherein R^1 and R^2 are each independently selected from hydrogen; hydroxy; amino; C_{1-6}alkyl; C_{1-6}alkyloxy; C_{1-6}alkylcarbonyl; C_{1-6}alkyloxycarbonyl; Ar^1; mono- or di(C_{1-6}alkyl)amino; mono- or di(C_{1-6}alkyl)aminocarbonyl; dihydro-2(3*H*)-furanone; C_{1-6}alkyl substituted with one or two substituents each independently selected from amino, imino, aminocarbonyl, aminocarbonylamino, hydroxy, hydroxyC_{1-6}alkyloxy, carboxyl, mono- or di(C_{1-6}alkyl)amino, C_{1-6}alkyloxycarbonyl and thienyl; or

R^1 and R^2 taken together may form pyrrolidinyl, piperidinyl, morpholinyl, azido or mono- or di(C_{1-6}alkyl)aminoC_{1-4}alkylidene;

R^3 is hydrogen, Ar^1, C_{1-6}alkylcarbonyl, C_{1-6}alkyl, C_{1-6}alkyloxycarbonyl, C_{1-6}alkyl substituted with C_{1-6}alkyloxycarbonyl; and

R^4, R^5, R^7 and R^8 are each independently selected from hydrogen, hydroxy, halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl or trihalomethyloxy;

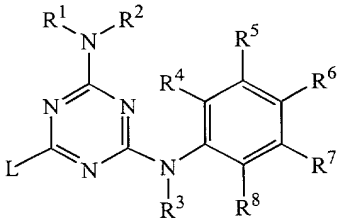
R^6 is selected from cyano or aminocarbonyl;

L is C_{1-10}alkyl; C_{3-10}alkenyl; C_{3-10}alkynyl; C_{3-7}cycloalkyl; or

L is C_{1-10}alkyl substituted with one or two substituents independently selected from C_{3-7}cycloalkyl; indolyl or indolyl substituted with one, two, three or four substituents each independently selected from halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, C_{1-6}alkylcarbonyl; phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, hydroxy, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, C_{1-6}alkylcarbonyl; and,

Ar^1 is phenyl, or phenyl substituted with one, two or three substituents each independently selected from halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, nitro or trifluoromethyl;
and (b) another antiretroviral compound, as a combined preparation for simultaneous, separate or sequential use in anti-HIV treatment.

17. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as active ingredients (a) a compound of formula (I)



(I)

wherein R^1 and R^2 are each independently selected from hydrogen; hydroxy; amino; C_{1-6}alkyl; C_{1-6}alkyloxy; C_{1-6}alkylcarbonyl; C_{1-6}alkyloxycarbonyl; Ar^1; mono- or di(C_{1-6}alkyl)amino; mono- or di(C_{1-6}alkyl)aminocarbonyl; dihydro-2(3*H*)-furanone; C_{1-6}alkyl substituted with one or two substituents each independently selected from amino, imino, aminocarbonyl, aminocarbonylamino, hydroxy, hydroxyC_{1-6}alkyloxy, carboxyl, mono- or di(C_{1-6}alkyl)amino, C_{1-6}alkyloxycarbonyl and thienyl; or

R^1 and R^2 taken together may form pyrrolidinyl, piperidinyl, morpholinyl, azido or mono- or di(C_{1-6}alkyl)aminoC_{1-4}alkylidene;

R^3 is hydrogen, Ar^1, C_{1-6}alkylcarbonyl, C_{1-6}alkyl, C_{1-6}alkyloxycarbonyl, C_{1-6}alkyl substituted with C_{1-6}alkyloxycarbonyl; and

R^4, R^5, R^7 and R^8 are each independently selected from hydrogen, hydroxy, halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl or trihalomethyloxy;

R^6 is selected from cyano or aminocarbonyl;

L is C_{1-10}alkyl; C_{3-10}alkenyl; C_{3-10}alkynyl; C_{3-7}cycloalkyl; or

L is C_{1-10}alkyl substituted with one or two substituents independently selected from C_{3-7}cycloalkyl; indolyl or indolyl substituted with one, two, three or four substituents each independently selected from halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, C_{1-6}alkylcarbonyl; phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, hydroxy, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, C_{1-6}alkylcarbonyl; and,

Ar^1 is phenyl, or phenyl substituted with one, two or three substituents each independently selected from halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, nitro or trifluoromethyl;

and (b) another antiretroviral compound.

18. A method of treating a subject suffering from HIV (Human Immunodeficiency Virus) infection comprising administering to the subject a therapeutically effective amount of the compound of claim 1.

REMARKS

Claims 1-17 are pending in the instant application. By the above amendments, Claims 5, 7-10, 13 and 15 have been canceled without prejudice, Claims 1-4, 6, 11-12, 14 and 16-17 amended and new Claim 18 added. Support for new claim 18 is found on page 14, lines 11-14 of the specification as filed. After entry of the amendments, Claims 1-4, 6, 11-12, 14 and 16-18 will remain pending and under consideration.

Early favorable action is respectfully requested.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached pages are captioned **"Version with Markings to Show Changes Made"**.

Respectfully submitted,

Mary A. Appolina

Mary A. Appolina
Attorney for Applicants
Reg. No. 34,087

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New Brunswick, NJ 08933-7003
(732) 524-3742
Dated: November 15, 2001

Version with Markings to Show Changes Made

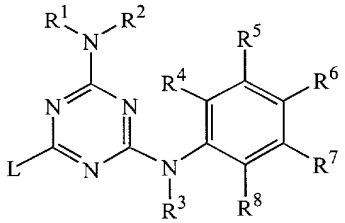
In the Specification:

On page 1, between the Title of the Invention and line 4 of the specification, add the following new paragraph:

This application is a divisional of prior application U.S. Serial No. 09/938,602, filed September 26, 1997, which claims priority from United States provisional application Serial No. 60/027,260, filed October 1, 1996, the contents of which are hereby incorporated by reference.

In the Claims:

1. A compound of formula



(I')

a pharmaceutically acceptable acid addition salt or a stereochemically isomeric form thereof, wherein

R^1 and R^2 are each independently selected from hydrogen; hydroxy; amino; C_{1-6}alkyl; C_{1-6}alkyloxy; C_{1-6}alkylcarbonyl; C_{1-6}alkyloxycarbonyl; Ar^1; mono- or di(C_{1-6}alkyl)amino; mono- or di(C_{1-6}alkyl)aminocarbonyl; dihydro-2(3*H*)-furanone; C_{1-6}alkyl substituted with one or two substituents each independently selected from amino, imino, aminocarbonyl, aminocarbonylamino, hydroxy, hydroxyC_{1-6}alkyloxy, carboxyl, mono- or di(C_{1-6}alkyl)amino, C_{1-6}alkyloxycarbonyl and thienyl; or

R^1 and R^2 taken together may form pyrrolidinyl, piperidinyl, morpholinyl, azido or mono- or di(C_{1-6}alkyl)aminoC_{1-4}alkylidene;

R^3 is hydrogen, Ar^1, C_{1-6}alkylcarbonyl, C_{1-6}alkyl, C_{1-6}alkyloxycarbonyl, C_{1-6}alkyl substituted with C_{1-6}alkyloxycarbonyl; and

R^4, R^5, ~~R^6~~, R^7 and R^8 are each independently selected from hydrogen, hydroxy, halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl or trihalomethyloxy ;

R^6 is aminocarbonyl; or

L is C_{1-10}alkyl substituted with one or two substituents independently selected from C_{3-7}cycloalkyl; indolyl or indolyl substituted with one, two, three or four substituents each independently selected from halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, C_{1-6}alkylcarbonyl; phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, hydroxy, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, C_{1-6}alkylcarbonyl; and,

Ar^1 is phenyl, or phenyl substituted with one, two or three substituents each independently selected from halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, nitro or trifluoromethyl~~;~~

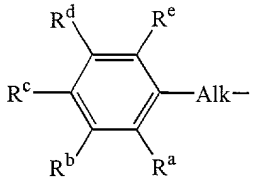
~~with the proviso that the following compounds~~

~~Co. No.~~	~~Alk~~	~~R^1/R^2~~	~~R^3~~	~~R^4~~	~~R^5~~	~~R^6~~	~~R^7~~	~~R^8~~
~~a~~	~~1-(4-(2-methylpropyl)phenyl)ethyl~~	~~H/H~~	~~H~~	~~CH_3~~	~~H~~	~~H~~	~~H~~	~~H~~
~~b~~	~~1-(4-(2-methylpropyl)phenyl)ethyl~~	~~H/H~~	~~H~~	~~H~~	~~H~~	~~NO_2~~	~~H~~	~~H~~
~~c~~	~~1-(4-(2-methylpropyl)phenyl)ethyl~~	~~H/H~~	~~C_6H_5~~	~~H~~	~~H~~	~~H~~	~~H~~	~~H~~
~~d~~	~~1-(4-(2-methylpropyl)phenyl)ethyl~~	~~H/H~~	~~H~~	~~NO_2~~	~~H~~	~~CH_3~~	~~H~~	~~H~~

e	1-(4-(2-methylpropyl)phenyl)ethyl	H/H	H	H	H	NH_2	H	H
f	4-(2-methylpropyl)phenylmethyl	H/H	H	H	CF_3	H	H	H
g	1-(4-(2-methylpropyl)phenyl)ethyl	H/H	H	H	H	Cl	H	H
h	4-(2-methylpropyl)phenylmethyl	H/H	H	H	H	H	H	H
i	3,4-dimethoxyphenylmethyl	H/H	H	H	H	H	H	H
j	2,3-dimethoxyphenylmethyl	H/H	H	H	H	H	H	H
k	3,4-diethoxyphenylmethyl	H/H	H	H	H	H	H	H
l	2-(3,5-(1,1-dimethylethyl)-4-hydroxy-phenyl)ethyl	H/H	H	H	H	H	H	H
m	2-(3,5-(1,1-dimethylethyl)-4-hydroxy-phenyl)ethyl	H/H	H	H	t-Bu	OH	t-Bu	H
n	phenylmethyl	H/H	H	CH_3	H	H	H	H
o	phenylmethyl	H/H	H	H	H	H	H	H

are not included.

2. A compound according to claim 1 wherein R^1 and R^2 are each independently selected from hydrogen, C_{1-6}alkyl, Ar^1 or mono- or di(C_{1-6}alkyl)aminocarbonyl; or R^1 and R^2 taken together may form pyrrolidinyl, piperidinyl or morpholinyl; R^3 is hydrogen, C_{1-6}alkyl or Ar^1; and Ar^1 is phenyl, or phenyl substituted with one, two or three substituents each independently selected from halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, nitro or trifluoromethyl; and
L is a radical of formula



wherein Alk is C_{1-6}alkanediyl;

R^a, R^b, R^c, R^d, R^e, R^4, R^5, ~~R^6,~~ R^7 and R^8 are each independently selected from hydrogen, halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl or trihalomethyloxy; or

R^a and R^b taken together may form a bivalent radical of formula

-CH=CH-NR^9- (a-1),

-NR^9-CH=CH- (a-2),

wherein R^9 is hydrogen or C_{1-4}alkyl.

3. A compound according to claim ~~1 or~~ 2 wherein L is C_{3-10}alkenyl or C_{1-2}alkyl substituted with one or two substituents independently selected from C_{3-7}cycloalkyl; indolyl or indolyl substituted with one, two, three or four substituents each independently selected from halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, C_{1-6}alkylcarbonyl; phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, hydroxy, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, C_{1-6}alkylcarbonyl.

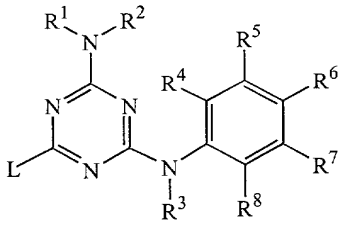
4. A compound according to ~~any one of claims 1 to~~ claim 3 wherein L is 2,6-dichlorophenylmethyl.

7. A compound according to claim 4 ~~any one of claims 1 to 5~~ wherein NR^1R^2 is other than amino.

11. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically active amount of a compound as claimed ~~in any one of claims~~ claim 1 ~~to 7~~.

12. A process for preparing a pharmaceutical composition ~~as claimed in claim 10 characterized in that~~ comprising intimately mixing a therapeutically effective amount of a compound as claimed in claim 1 ~~any one of claims 1 to 7 is intimately mixed~~ with a pharmaceutically acceptable carrier.

15. The combination of a compound of formula (I)



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wherein R^1 and R^2 are each independently selected from hydrogen; hydroxy; amino; C_{1-6}alkyl; C_{1-6}alkyloxy; C_{1-6}alkylcarbonyl; C_{1-6}alkyloxycarbonyl; Ar^1; mono- or di(C_{1-6}alkyl)amino; mono- or di(C_{1-6}alkyl)aminocarbonyl; dihydro-2(3*H*)-furanone; C_{1-6}alkyl substituted with one or two substituents each independently selected from amino, imino, aminocarbonyl, aminocarbonylamino, hydroxy, hydroxyC_{1-6}alkyloxy, carboxyl, mono- or di(C_{1-6}alkyl)amino, C_{1-6}alkyloxycarbonyl and thienyl; or

R^1 and R^2 taken together may form pyrrolidinyl, piperidinyl, morpholinyl, azido or mono- or di(C_{1-6}alkyl)aminoC_{1-4}alkylidene;

R^3 is hydrogen, Ar^1, C_{1-6}alkylcarbonyl, C_{1-6}alkyl, C_{1-6}alkyloxycarbonyl, C_{1-6}alkyl substituted with C_{1-6}alkyloxycarbonyl; and

R^4, R^5, R^7 and R^8 are each independently selected from hydrogen, hydroxy, halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl or trihalomethyloxy;

R^6 is selected from cyano or aminocarbonyl;

L is C_{1-10}alkyl; C_{3-10}alkenyl; C_{3-10}alkynyl; C_{3-7}cycloalkyl; or

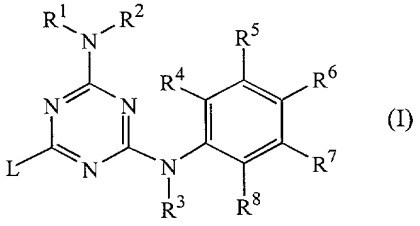
L is C_{1-10}alkyl substituted with one or two substituents independently selected from C_{3-7}cycloalkyl; indolyl or indolyl substituted with one, two, three or four

substituents each independently selected from halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, C_{1-6}alkylcarbonyl; phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, hydroxy, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, C_{1-6}alkylcarbonyl; and,

Ar^1 is phenyl, or phenyl substituted with one, two or three substituents each independently selected from halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, nitro or trifluoromethyl;

~~as defined in claim 9~~ and another antiretroviral compound.

16. A product containing (a) a compound of formula (I)



(I)

wherein R^1 and R^2 are each independently selected from hydrogen; hydroxy; amino; C_{1-6}alkyl; C_{1-6}alkyloxy; C_{1-6}alkylcarbonyl; C_{1-6}alkyloxycarbonyl; Ar^1; mono- or di(C_{1-6}alkyl)amino; mono- or di(C_{1-6}alkyl)aminocarbonyl; dihydro-2(3*H*)-furanone; C_{1-6}alkyl substituted with one or two substituents each independently selected from amino, imino, aminocarbonyl, aminocarbonylamino, hydroxy, hydroxyC_{1-6}alkyloxy, carboxyl, mono- or di(C_{1-6}alkyl)amino, C_{1-6}alkyloxycarbonyl and thienyl; or

R^1 and R^2 taken together may form pyrrolidinyl, piperidinyl, morpholinyl, azido or mono- or di(C_{1-6}alkyl)aminoC_{1-4}alkylidene;

R^3 is hydrogen, Ar^1, C_{1-6}alkylcarbonyl, C_{1-6}alkyl, C_{1-6}alkyloxycarbonyl, C_{1-6}alkyl substituted with C_{1-6}alkyloxycarbonyl; and

R^4, R^5, R^7 and R^8 are each independently selected from hydrogen, hydroxy, halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano,

aminocarbonyl, nitro, amino, trihalomethyl or trihalomethyloxy;

R^6 is selected from cyano or aminocarbonyl;

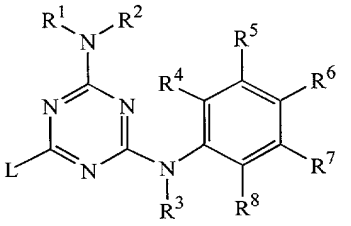
L is C_{1-10}alkyl; C_{3-10}alkenyl; C_{3-10}alkynyl; C_{3-7}cycloalkyl; or

L is C_{1-10}alkyl substituted with one or two substituents independently selected from C_{3-7}cycloalkyl; indolyl or indolyl substituted with one, two, three or four substituents each independently selected from halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, C_{1-6}alkylcarbonyl; phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, hydroxy, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, C_{1-6}alkylcarbonyl; and,

Ar^1 is phenyl, or phenyl substituted with one, two or three substituents each independently selected from halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, nitro or trifluoromethyl;

~~as defined in claim 9,~~ and (b) another antiretroviral compound, as a combined preparation for simultaneous, separate or sequential use in anti-HIV treatment.

17. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as active ingredients (a) a compound of formula (I)



(I)

wherein R^1 and R^2 are each independently selected from hydrogen; hydroxy; amino; C_{1-6}alkyl; C_{1-6}alkyloxy; C_{1-6}alkylcarbonyl; C_{1-6}alkyloxycarbonyl; Ar^1; mono- or di(C_{1-6}alkyl)amino; mono- or di(C_{1-6}alkyl)aminocarbonyl; dihydro-2(3*H*)-furanone; C_{1-6}alkyl substituted with one or two substituents each independently selected from amino, imino, aminocarbonyl, aminocarbonylamino, hydroxy,

hydroxyC_{1-6}alkyloxy, carboxyl, mono- or di(C_{1-6}alkyl)amino, C_{1-6}alkyloxycarbonyl and thienyl; or

R^1 and R^2 taken together may form pyrrolidinyl, piperidinyl, morpholinyl, azido or mono- or di(C_{1-6}alkyl)aminoC_{1-4}alkylidene;

R^3 is hydrogen, Ar^1, C_{1-6}alkylcarbonyl, C_{1-6}alkyl, C_{1-6}alkyloxycarbonyl, C_{1-6}alkyl substituted with C_{1-6}alkyloxycarbonyl; and

R^4, R^5, R^7 and R^8 are each independently selected from hydrogen, hydroxy, halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl or trihalomethyloxy;

R^6 is selected from cyano or aminocarbonyl;

L is C_{1-10}alkyl; C_{3-10}alkenyl; C_{3-10}alkynyl; C_{3-7}cycloalkyl; or

L is C_{1-10}alkyl substituted with one or two substituents independently selected from C_{3-7}cycloalkyl; indolyl or indolyl substituted with one, two, three or four substituents each independently selected from halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, C_{1-6}alkylcarbonyl; phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, hydroxy, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, C_{1-6}alkylcarbonyl; and,

Ar^1 is phenyl, or phenyl substituted with one, two or three substituents each independently selected from halo, C_{1-6}alkyl, C_{1-6}alkyloxy, cyano, nitro or trifluoromethyl;

~~as defined in claim 9,~~ and (b) another antiretroviral compound.

Add new Claim 18 as follows:

18. A method of treating a subject suffering from HIV (Human Immunodeficiency Virus) infection comprising administering to the subject a therapeutically effective amount of the compound of claim 1.